Synthesis and lipase-catalyzed resolution of 5-(hydroxymethyl)-1,3-dioxolan-4-ones

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1996

Enantiomeric excess Determination of Compounds **2a,b**, **9-12** resolved by Candida antarctia lipase

Resolved by HPLC on Daicel OJ column

Compound	Solvent	Flow rate (ml/min)	t_{R1} (min)	t_{R2} (min)
2a	hexane/ipa 8:2	1.0	7.5(major,S)	12.4(minor,R)
11a	hexane/ipa 8:2	1.0	10.6(major,R)	14.9(minor,S)
2b	hexane/ipa 8:2	0.5	13.8(major)	45.2(minor)
11b	hexane/ipa 8:2	0.5	20.7(minor)	23.6(major)
10	hexane/ipa 9:1	0.5	19.5(major)	23.3(minor)
11d	hexane/ipa 8:2	1.0	7.1(major)	16.4(minor)
12	hexane/ipa 9:1	1.0	23.5(minor,R)	37.4(major,S)

Resolved by GC on FS-LIPODEX C column

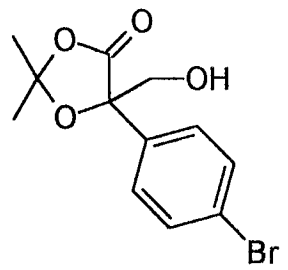
Compound	Carrier gas	Oven temp (°C)	t_{R1} (min)	t_{R2} (min)
9	He	125	164.8	172.2
11c	He	125	145.6	147.3

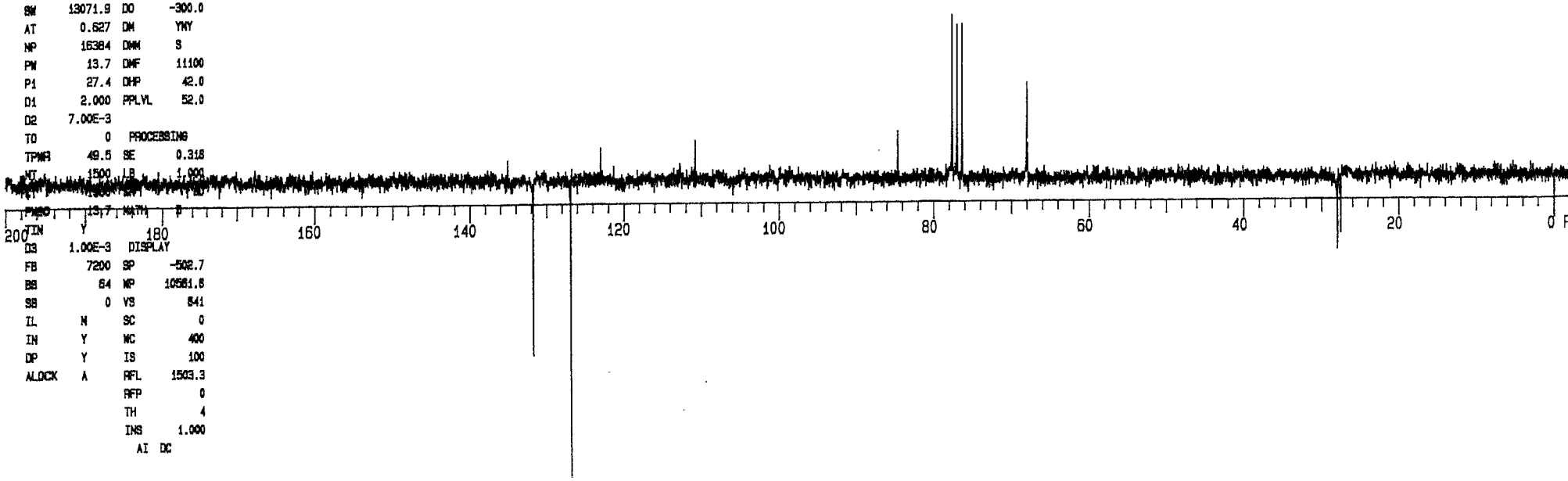
In general, conditions were optimized to perform the analysis of **2a,b** and the corresponding acetate **11** in a single run. Only for **10** did the components have to be separated prior to analysis by chromatography (silica, ether).

OF NAFT
SPECTRAL LINES FOR TH= 4.00
REL= 1503.3 RFP= 0

INDEX	FREQ	PPM	INTENSITY
01	6792.1	135.061	4.332
*02	6626.8	131.771	-42.009
*03	6380.6	126.877	-70.982
04	6187.3	123.033	3.757
05	5672.9	110.316	9.364
06	4264.7	84.820	11.286
07	3909.6	77.761	4.151
08	3903.6	77.622	38.983
09	3871.9	76.987	36.662
10	3839.7	76.353	36.740
11	3419.9	68.003	22.812
*12	1406.9	27.976	-18.471
*13	1384.9	27.539	-14.145
*14	-1.6	-0.031	-10.229

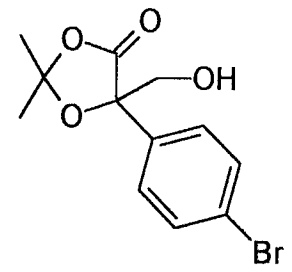
		DN	1.000
SW	13071.9	DO	-300.0
AT	0.627	DM	YNY
NP	16384	DMM	S
PW	13.7	DMF	11100
P1	27.4	DMP	42.0
D1	2.000	PPLVL	52.0
D2	7.00E-3		
TO	0	PROCESSING	
TPWR	49.5	SE	0.318
NT	1500	LB	1.000
[illegible]	[illegible]	[illegible]	[illegible]
PWRO	13.7	MATH	0
IN	Y		
D3	1.00E-3	DISPLAY	
FB	7200	SP	-502.7
BS	64	WP	10561.6
SB	0	VS	841
IL	N	SC	0
IN	Y	WC	400
DP	Y	IS	100
ALOCK	A	RFL	1503.3
		RFP	0
		TH	4
		INS	1.000
		AI	DC

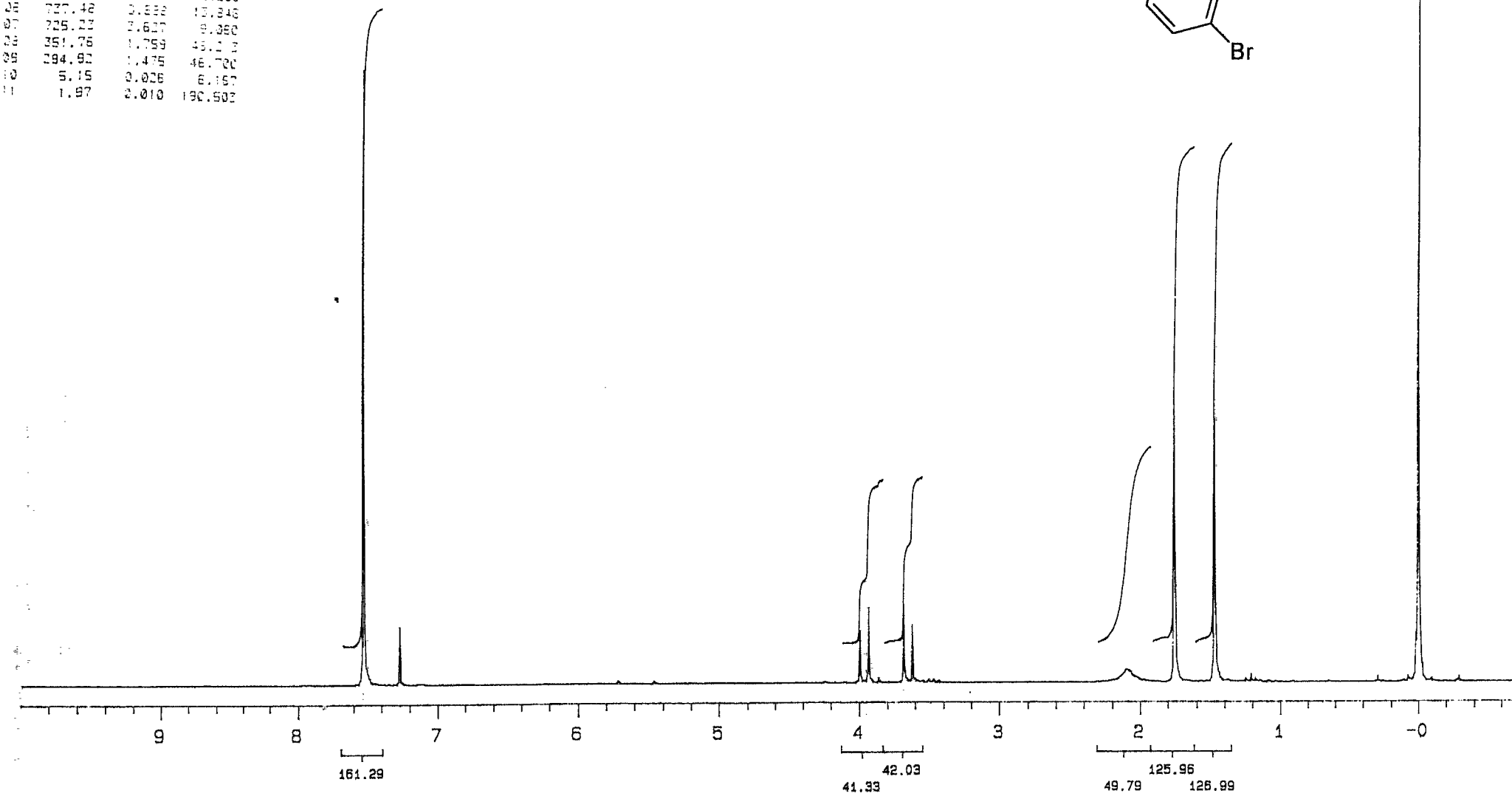




NOE NAFT
SPECTRAL LINES FOR TH= 4.00
RFL= 610.9 RFP= 0

INDEX	FREQ	PPM	INTENSITY
01	1507.13	2.527	121.145
02	1502.10	2.518	9.421
03	1454.82	2.439	11.218
04	799.92	1.300	0.579
05	797.72	1.339	12.106
06	727.42	1.220	13.846
07	725.23	1.217	8.380
08	351.76	1.759	45.123
09	294.92	1.475	46.720
10	5.15	0.026	6.157
11	1.97	0.010	190.502





ADF

RAL LINES FOR TH= 10.00

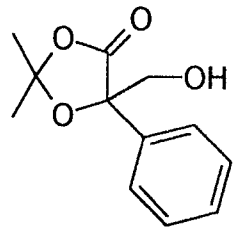
L= 1502.3 AFP= 0

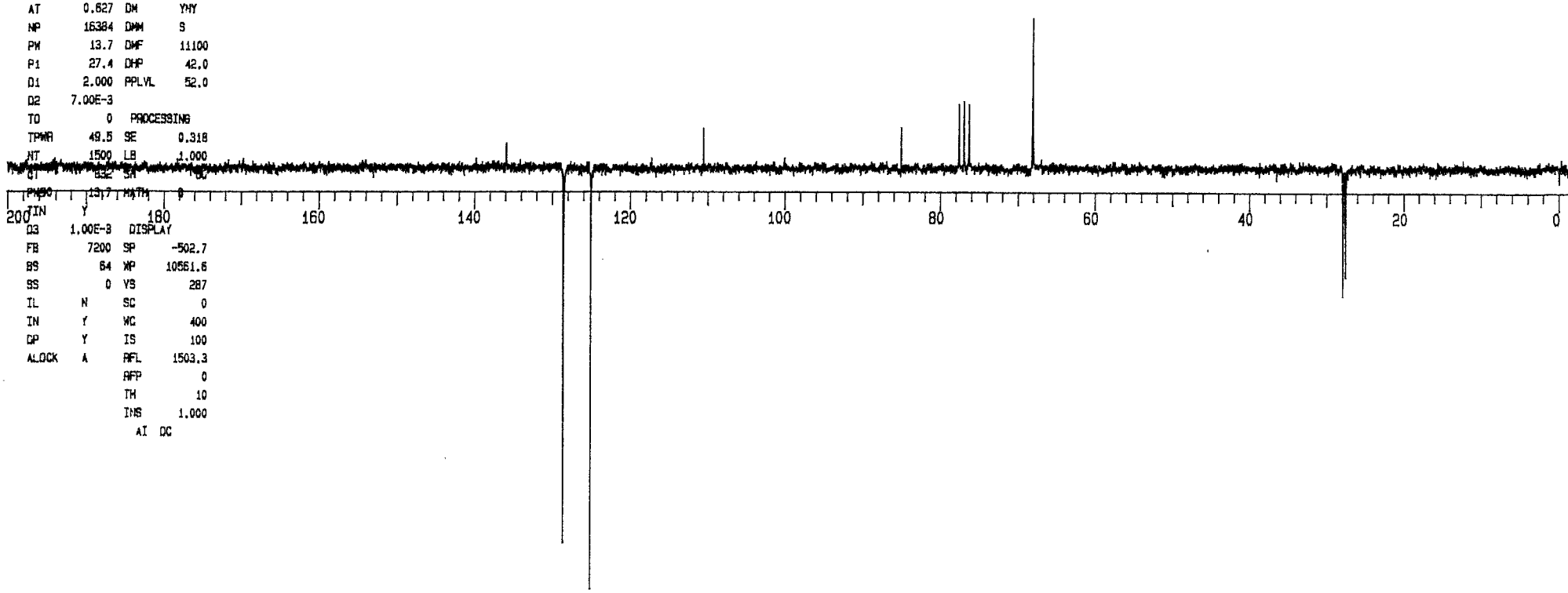
DEV	FREQ	PPM	INTENSITY
01	8455.9	123.566	-94.111
02	8239.1	120.064	-100.000
03	3905.2	57.054	15.399
04	3873.1	57.015	16.377
05	3841.1	56.381	15.687
06	3428.4	50.133	36.102
07	1404.0	27.919	-21.079
08	1395.3	27.557	-26.985

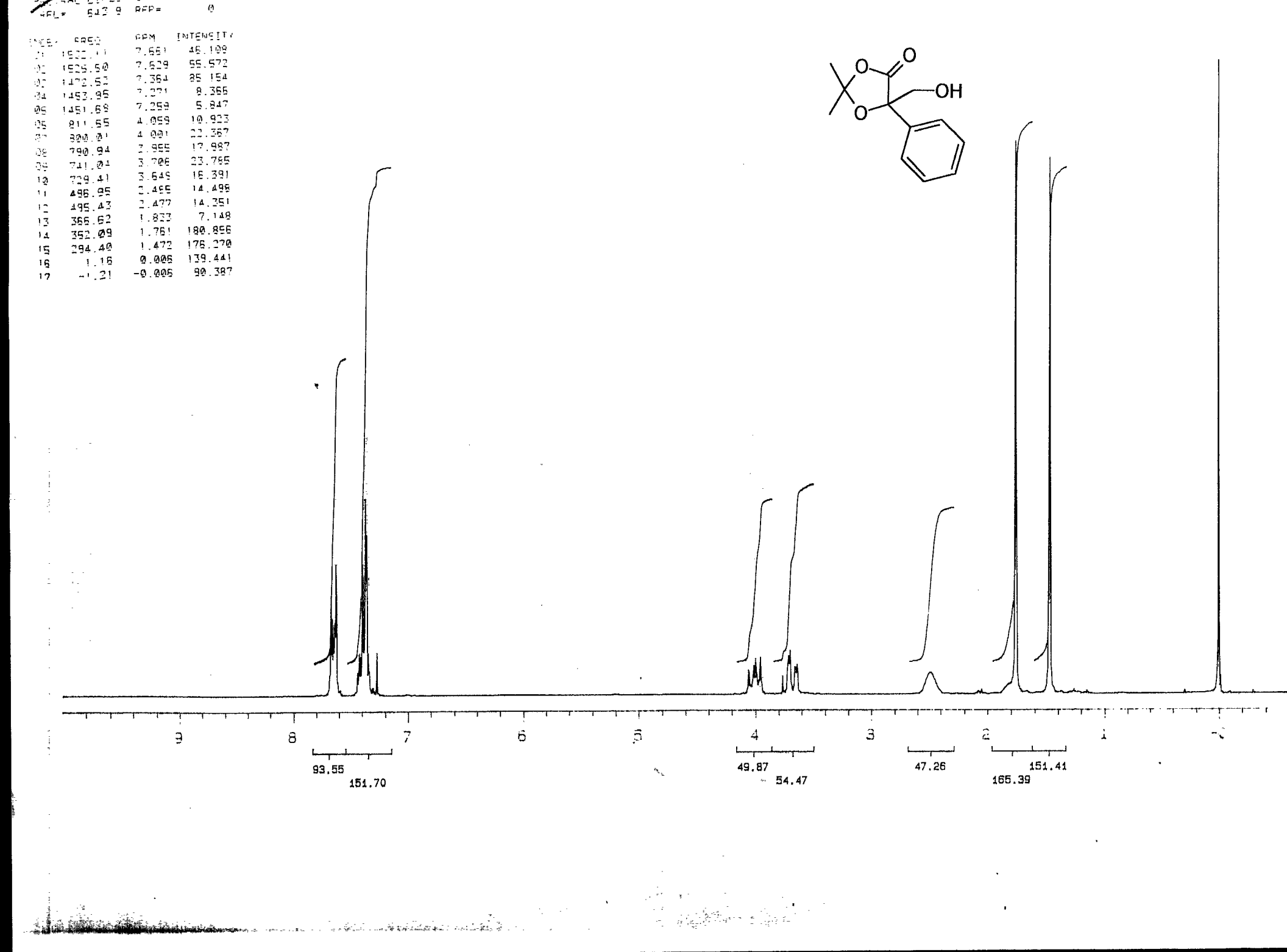
SOLVENT CDCL3

FILE ROBE02

ACQUISITION		DEC. S VT	
TN	13.000	DN	1.000
SW	13071.9	DO	-300.0
AT	0.627	DM	YNY
NP	16384	DMM	S
PW	13.7	DMF	11100
P1	27.4	DHP	42.0
D1	2.000	PPLVL	52.0
D2	7.00E-3		
TO	0	PROCESSING	
TPWR	49.5	SE	0.318
NT	1500	LB	1.000
CT	832	SN	DC
PWR0	13.7	MATH	0
TIN	Y		
D3	1.00E-3	DISPLAY	
FB	7200	SP	-502.7
BS	64	WP	10561.6
SS	0	VS	287
IL	N	SC	0
IN	Y	WC	400
DP	Y	IS	100
ALOCK	A	RFL	1503.3
		RFP	0
		TH	10
		INS	1.000
		AI DC	






INDEX FREQ PPM INTENSITY
01 1532.11 7.661 46.109
02 1525.50 7.629 55.572
03 1472.52 7.364 85.154
04 1453.96 7.271 8.366
05 1451.69 7.259 5.847
06 811.65 4.059 10.923
07 800.01 4.001 22.367
08 790.94 3.955 17.987
09 741.01 3.706 23.795
10 729.41 3.648 16.391
11 496.95 2.485 14.498
12 495.43 2.477 14.351
13 366.62 1.833 7.148
14 352.09 1.761 180.856
15 294.40 1.472 176.270
16 1.16 0.006 139.441
17 -1.21 -0.005 90.387
OH
9
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5
4
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2
1
93.55
151.70
49.87
54.47
47.26
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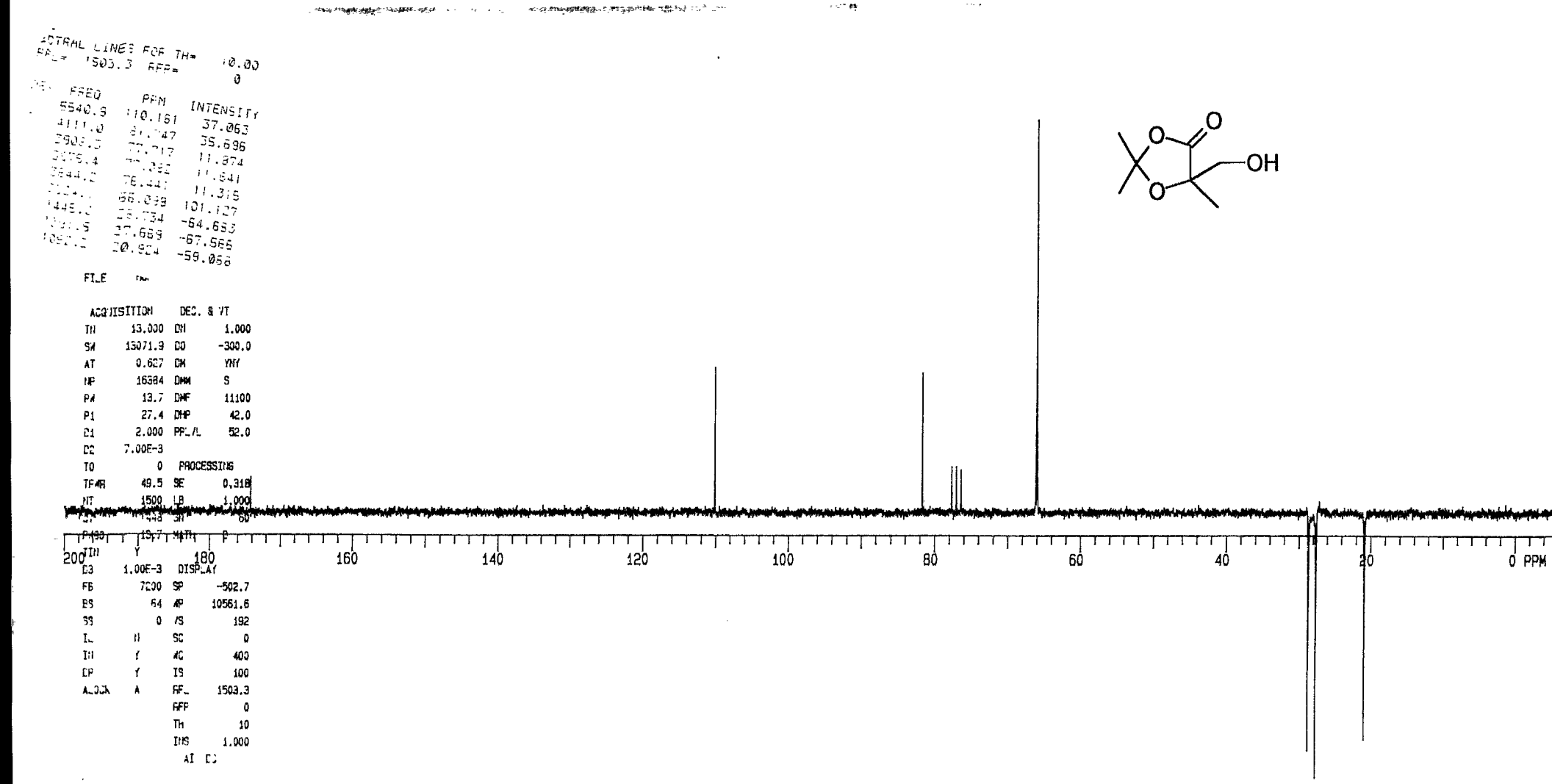
151.41



SPECTRAL LINES FOR TH=
RFL= 1503.3 RFP= 0.00
0

FREQ	PPM	INTENSITY
5540.9	110.161	37.063
4111.0	81.747	35.696
3903.3	77.717	11.874
3875.4	77.282	11.841
3844.2	76.447	11.315
3548.1	66.039	101.127
1445.2	28.734	-64.683
1381.5	27.669	-67.566
1052.2	20.924	-59.058

FILE

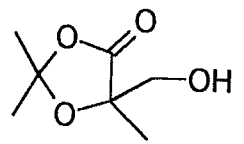
ACQUISITION		DEC. & VT	
TN	13.000	DN	1.000
SW	13071.9	DO	-300.0
AT	0.627	DM	YNY
NP	16384	DMM	S
PW	13.7	DMF	11100
P1	27.4	DMP	42.0
D1	2.000	PPL/L	52.0
D2	7.00E-3		
TO	0	PROCESSING	
TPWR	49.5	SE	0.318
NT	1500	LB	1.000
CT	448	GN	60
P180	19.7	MATH	P
HIN	Y		
D3	1.00E-3	DISPLAY	
FB	7200	SP	-502.7
BS	64	WP	10561.6
SS	0	WS	192
LB	N	SC	0
IN	Y	WC	400
DP	Y	IS	100
ALOCK	A	RFL	1503.3
		RFP	0
		TH	10
		INS	1.000

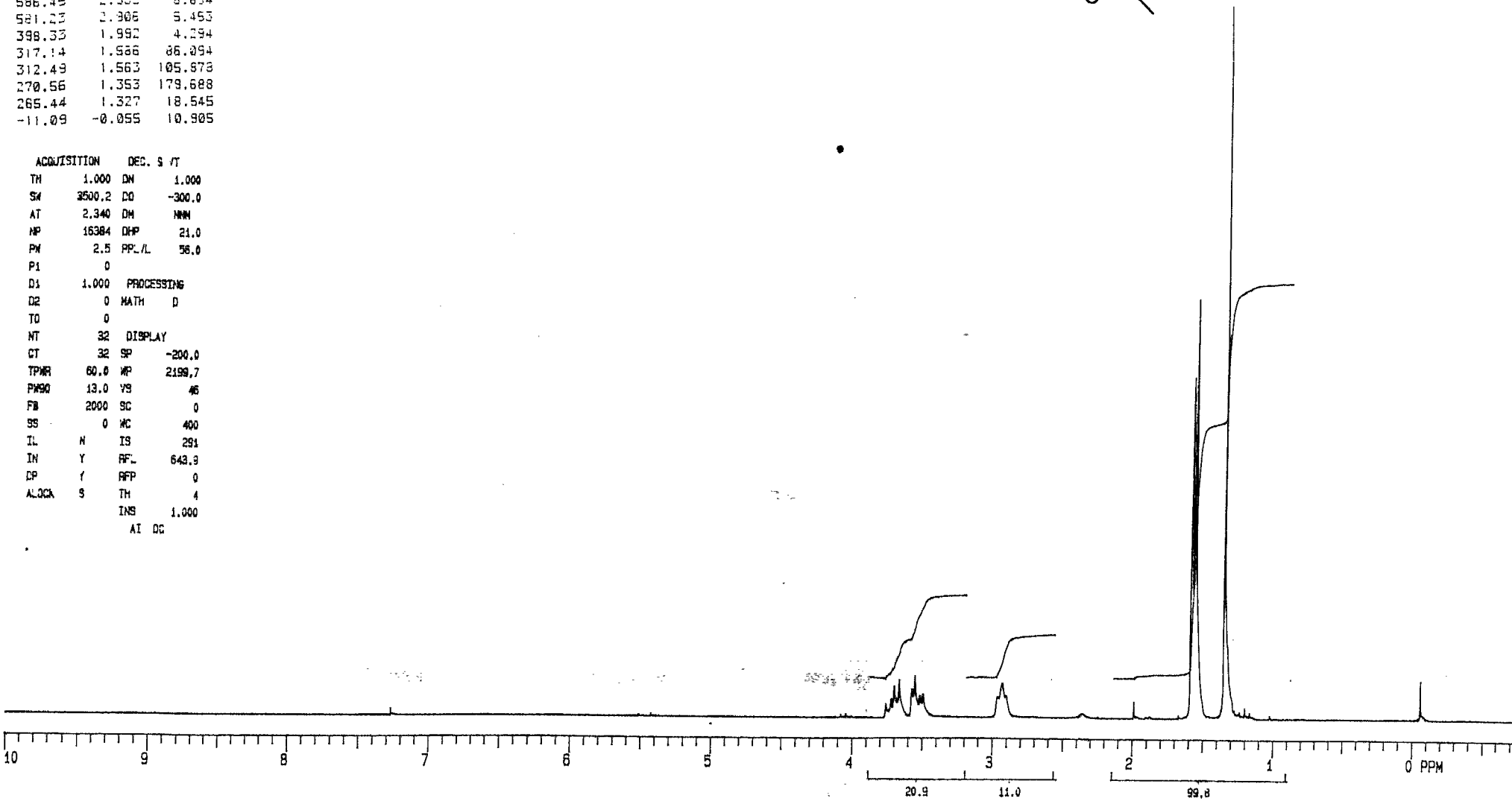
AI D

SOL= 643.9 RFP= 0

INDEX	FREQ	PPM	INTENSITY
01	744.69	3.725	4.421
02	740.26	3.702	7.757
03	732.92	3.665	9.278
04	715.50	3.578	7.035
05	710.80	3.554	10.441
06	703.77	3.519	5.381
07	699.07	3.496	5.796
08	593.10	2.968	5.216
09	586.45	2.933	8.634
10	581.23	2.906	5.453
11	398.33	1.992	4.294
12	317.14	1.586	86.094
13	312.49	1.563	105.873
14	270.56	1.353	179.688
15	265.44	1.327	18.545
16	-11.09	-0.055	10.905

ACQUISITION		DEC. S /T	
TM	1.000	DN	1.000
SW	3500.2	DO	-300.0
AT	2.340	DM	NNN
NP	16384	DHP	21.0
PW	2.5	PPL/L	56.0
P1	0		
D1	1.000	PROCESSING	
D2	0	MATH	D
TO	0		
NT	32	DISPLAY	
CT	32	SP	-200.0
TPWR	60.0	WP	2199.7
PW90	13.0	VS	46
FB	2000	SC	0
SS	0	WC	400
IL	N	IS	291
IN	Y	RFL	643.9
DP	f	RFP	0
ALOCK	S	TH	4
		INS	1.000
		AI DC	



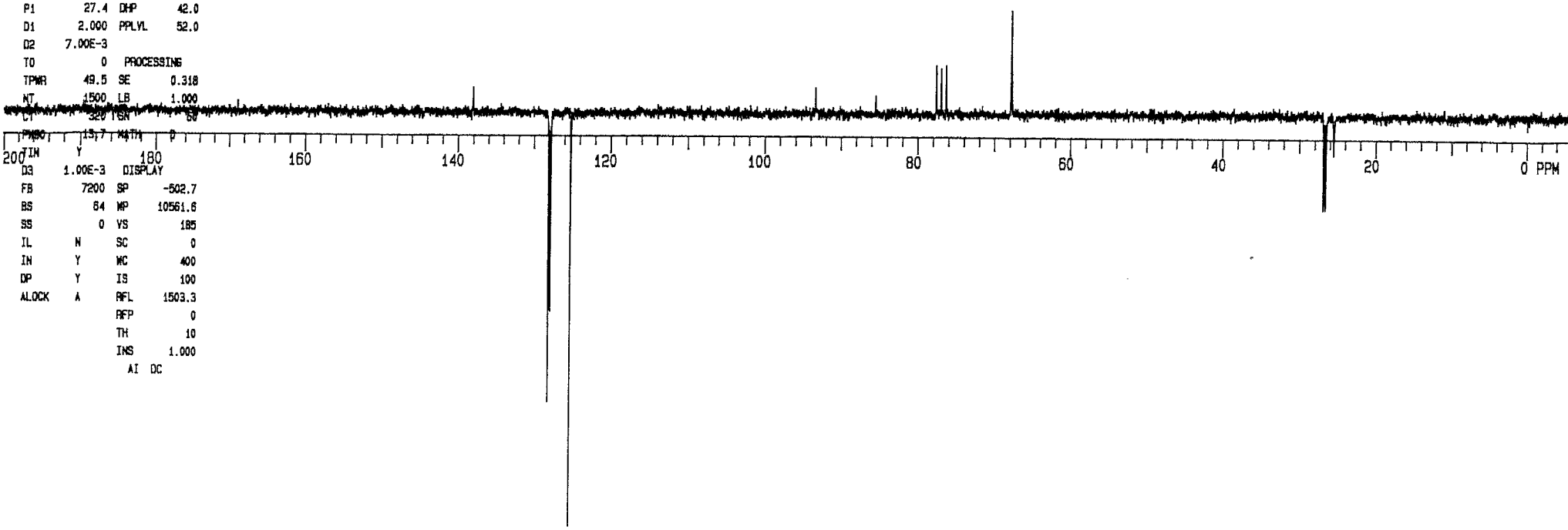


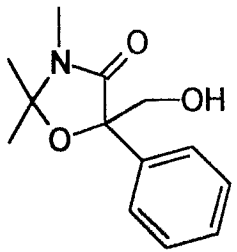
-OTRAL LINES FOR TH= 10.00
RFL= 1503.3 RFP= 0

INDEX	FREQ	PPM	INTENSITY
12	6444.5	129.150	-73.584
33	6431.3	127.992	-48.340
13	6299.3	125.255	-100.092
4	3905.5	77.692	12.093
5	3874.9	77.051	11.201
6	3842.7	76.412	12.221
7	3414.5	67.897	27.240
8	1352.9	26.900	-23.703
9	1330.3	25.611	-24.259

SOLVENT
FILE HOFA02

ACQUISITION		DEC. & VT	
TN	13.000	DN	1.000
SW	13071.9	DO	-300.0
AT	0.627	DM	YNY
NP	16384	DMM	S
PW	13.7	DMF	11100
P1	27.4	DHP	42.0
D1	2.000	PPLVL	52.0
D2	7.00E-3		
TO	0	PROCESSING	
TPWR	49.5	SE	0.318
NT	1500	LB	1.000
CT	320	TGN	60
PWR0	13.7	MATH	0
TIN	Y		
D3	1.00E-3	DISPLAY	
FB	7200	SP	-502.7
BS	64	WP	10561.6
SS	0	VS	185
IL	N	SC	0
IN	Y	WC	400
DP	Y	IS	100
ALOCK	A	RFL	1503.3
		RFP	0
		TH	10
		INS	1.000
		AI DC	

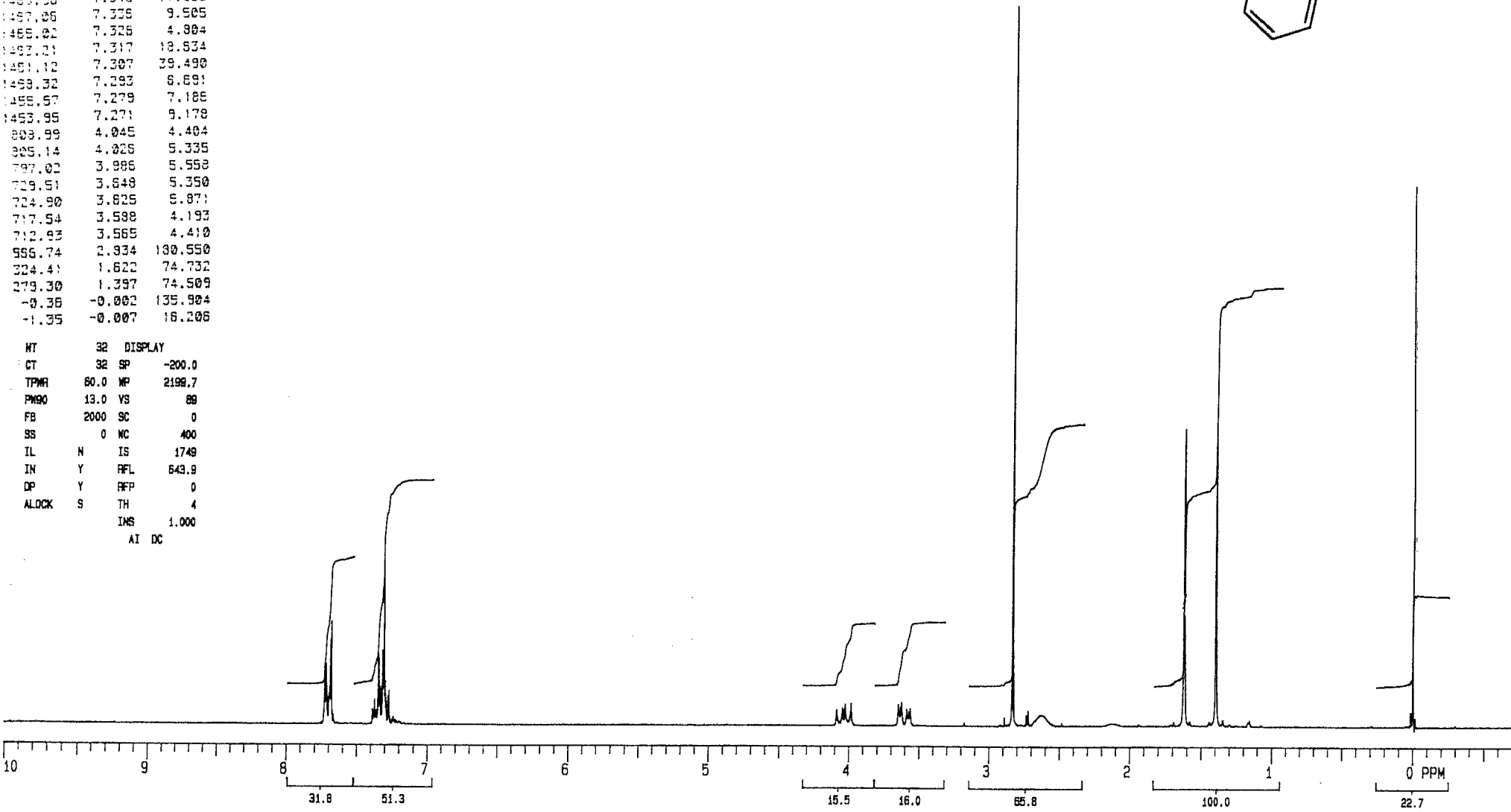




PEAKTRAL LINES FOR TH= 4.00
PFL= 643.9 RFP= 0

NO.	FREQ	PPM	INTENSITY
21	1548.02	7.731	15.987
22	1547.38	7.721	15.084
23	1541.94	7.711	6.711
24	1537.61	7.699	21.891
25	1535.29	7.682	25.709
26	1474.37	7.373	6.451
27	1469.96	7.345	17.660
28	1467.06	7.338	9.505
29	1465.02	7.326	4.804
30	1463.21	7.317	18.534
31	1461.12	7.307	39.490
32	1459.32	7.293	6.691
33	1455.67	7.279	7.186
34	1453.95	7.271	9.178
35	808.99	4.045	4.404
36	805.14	4.026	5.335
37	797.02	3.986	5.552
38	729.51	3.648	5.350
39	724.90	3.625	6.871
40	717.54	3.588	4.193
41	712.93	3.565	4.410
42	566.74	2.834	100.550
43	324.41	1.622	74.732
44	279.30	1.397	74.509
45	-0.36	-0.002	135.904
46	-1.35	-0.007	16.206

NT	32	DISPLAY	
CT	32	SP	-200.0
TPWR	60.0	WP	2199.7
PW90	13.0	VS	89
FB	2000	SC	0
SS	0	WC	400
IL	N	IS	1749
IN	Y	RFL	643.9
DP	Y	RFP	0
ALOCK	S	TH	4
		INS	1.000
		AI DC	

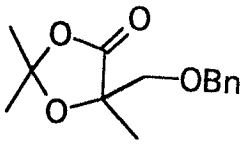


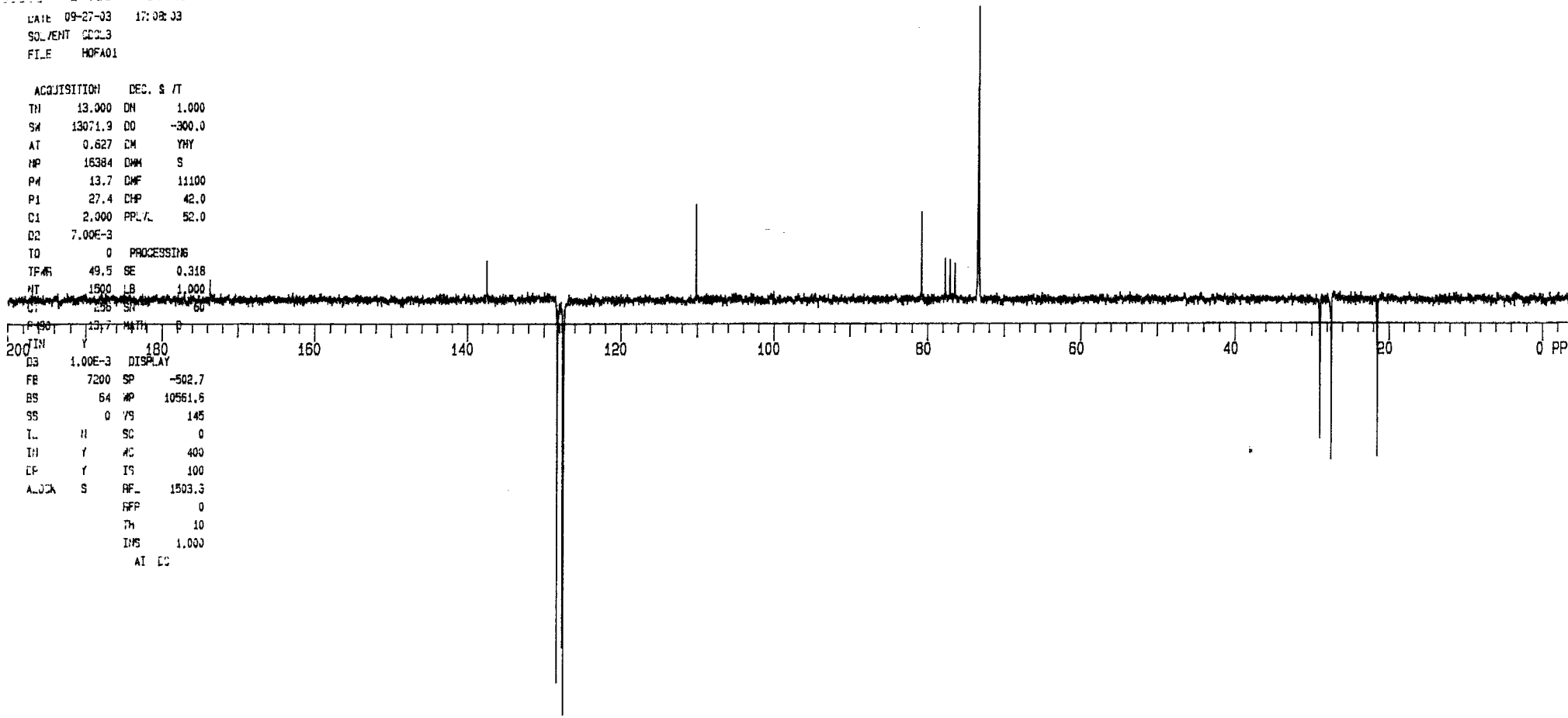
LINES FOR TH= 10.00
1503.3 RFP= 0

FREQ	PPM	INTENSITY
6155.1	129.351	-94.184
6112.2	127.666	-82.999
6102.1	127.504	-101.026
4949.3	110.181	22.052
4521.7	80.927	21.199
4431.5	77.401	70.525
1668.1	23.995	-74.642
1582.2	20.617	-28.542
1551.9	21.551	-38.427

DATE 09-27-03 17:08:33
SOLVENT CDCL3
FILE HOFA01

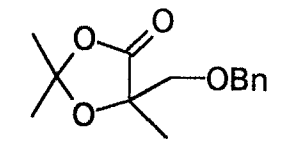
ACQUISITION		DEC. & /T	
TN	13.000	DN	1.000
SW	13071.9	DO	-300.0
AT	0.627	DM	YNY
NP	16384	DMM	S
PW	13.7	DMF	11100
P1	27.4	DMP	42.0
C1	2.000	PPLVL	52.0
D2	7.00E-3		
TO	0	PROCESSING	
TPWR	49.5	SE	0.318
NT	1500	LB	1.000
CT	256	SN	60
P180	13.7	MATH	0
FIN	Y		
D3	1.00E-3	DISPLAY	
FB	7200	SP	-502.7
BS	64	WP	10561.6
SS	0	VS	145
IL	N	SC	0
IN	Y	WC	400
DP	Y	IS	100
ALOCK	S	RF_	1503.3
		RFP	0
		TH	10
		INS	1.000
		AI DC	

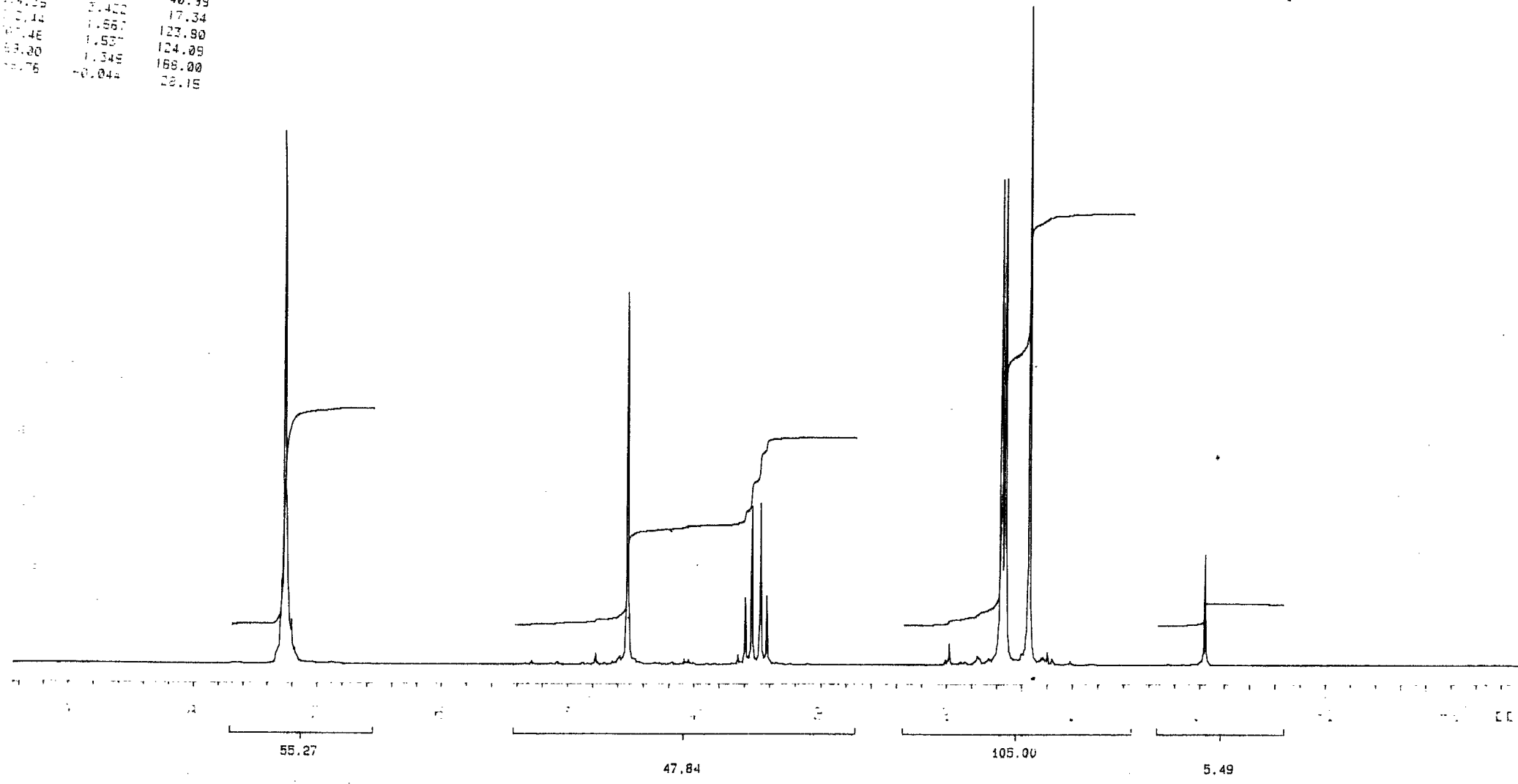


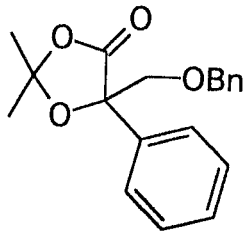


LINES FOR TH = 14.35
2108.40 , REF = 1451.82

FREQ	PPM	INTENSITY
1455.66	7.275	28.76
1451.82	7.260	136.01
905.28	4.527	94.68
718.54	3.593	16.93
709.22	3.542	40.21
694.97	3.473	40.99
684.35	3.422	17.34
375.44	1.867	123.90
367.46	1.527	124.09
363.30	1.345	168.00
359.76	-0.044	28.15



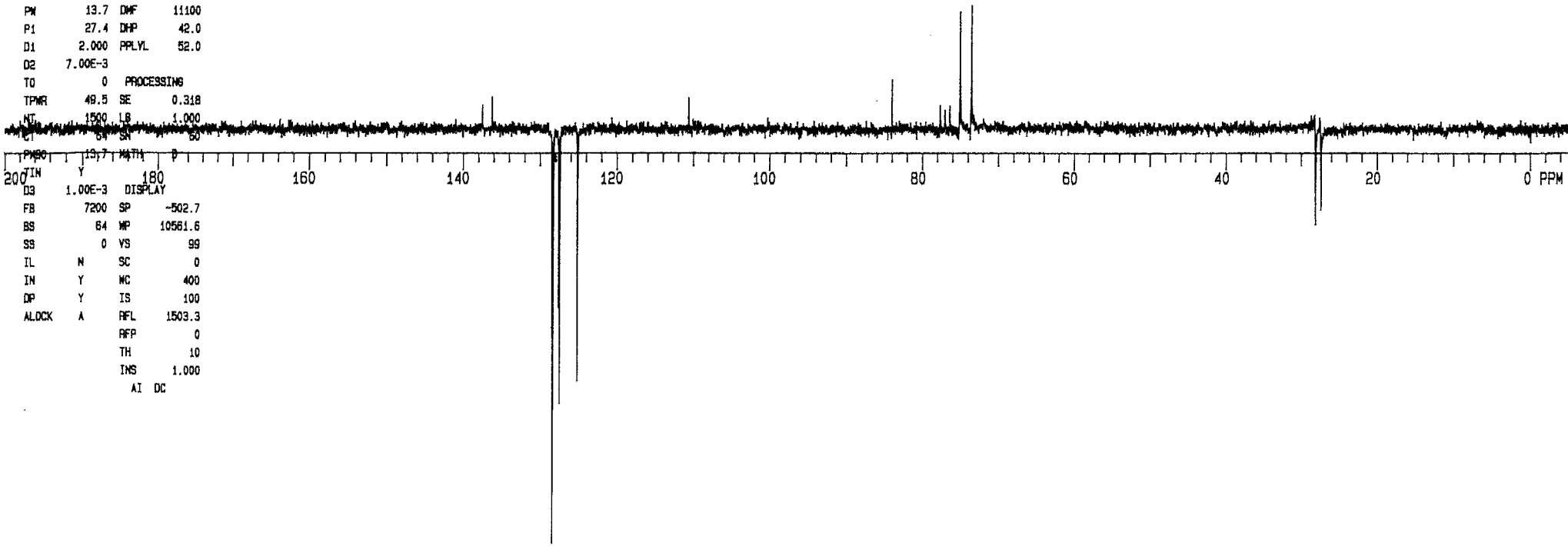




RAL LINES FOR TH= 10.00
L= 1503.3 RFP= 0

FREQ	PPM	INTENSITY
6480.4	128.523	-50.681
6460.0	128.456	-100.387
6435.8	128.383	-69.178
6420.2	127.886	-43.583
6412.2	127.505	-66.635
6388.3	126.201	-66.923
4229.1	84.036	12.108
3778.3	75.142	23.892
3722.9	73.652	30.242
1167.2	23.180	-23.292
1130.2	22.447	-19.534

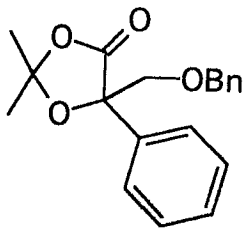
ACQUISITION		DEC. & VT	
TN	13.000	DN	1.000
SW	13071.9	DO	-300.0
AT	0.627	DM	YNY
NP	16384	DMM	S
PW	13.7	DMF	11100
P1	27.4	DHP	42.0
D1	2.000	PPLVL	52.0
D2	7.00E-3		
TO	0	PROCESSING	
TPWR	49.5	SE	0.318
NT	1500	LB	1.000
CT	64	SN	50
TPWR0	13.7	MATH	0
TIN	Y		
D3	1.00E-3	DISPLAY	
FB	7200	SP	-502.7
BS	64	WP	10561.6
SS	0	VS	99
IL	N	SC	0
IN	Y	WC	400
DP	Y	IS	100
ALOCK	A	RFL	1503.3
		RFP	0
		TH	10
		INS	1.000
		AI DC	

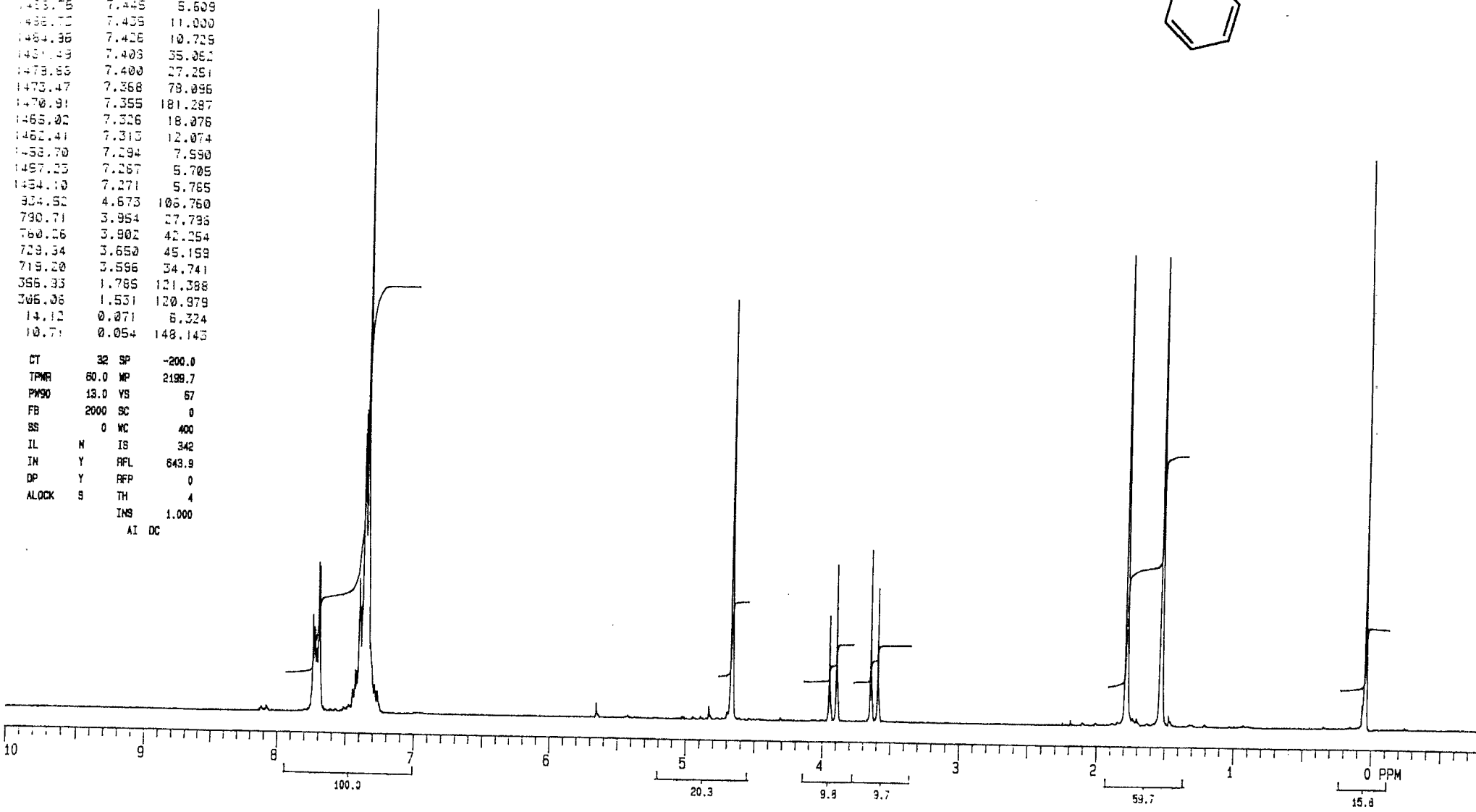


SPECTRAL LINES FOR TH= 4.00
RFL= 843.9 RFP= 0

	FREQ	PPM	INTENSITY
21	1549.01	7.746	26.207
22	1546.57	7.735	22.123
23	1542.74	7.719	16.453
24	1540.34	7.706	38.352
25	1535.22	7.687	37.612
26	1490.47	7.459	8.243
27	1488.78	7.446	6.609
28	1486.72	7.435	11.000
29	1484.36	7.426	10.729
30	1481.49	7.408	35.062
31	1478.65	7.400	27.291
32	1473.47	7.368	78.096
33	1470.91	7.355	181.287
34	1466.02	7.326	18.076
35	1462.41	7.313	12.074
36	1458.70	7.294	7.550
37	1457.23	7.287	5.705
38	1454.10	7.271	5.765
39	934.52	4.673	106.760
40	790.71	3.954	27.796
41	780.26	3.902	42.254
42	729.34	3.650	45.159
43	719.20	3.596	34.741
44	366.33	1.786	121.388
45	306.06	1.531	120.979
46	14.12	0.071	6.324
47	10.71	0.054	148.145

CT	32	SP	-200.0
TPWR	60.0	WP	2199.7
PW90	13.0	VS	67
FB	2000	SC	0
SS	0	WC	400
IL	N	IS	342
IN	Y	RFL	843.9
DP	Y	RFP	0
ALOCK	S	TH	4
		INS	1.000
		AI	DC



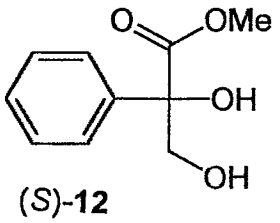


Channel 99EM | Date Processed 29/09/95 15:01:27

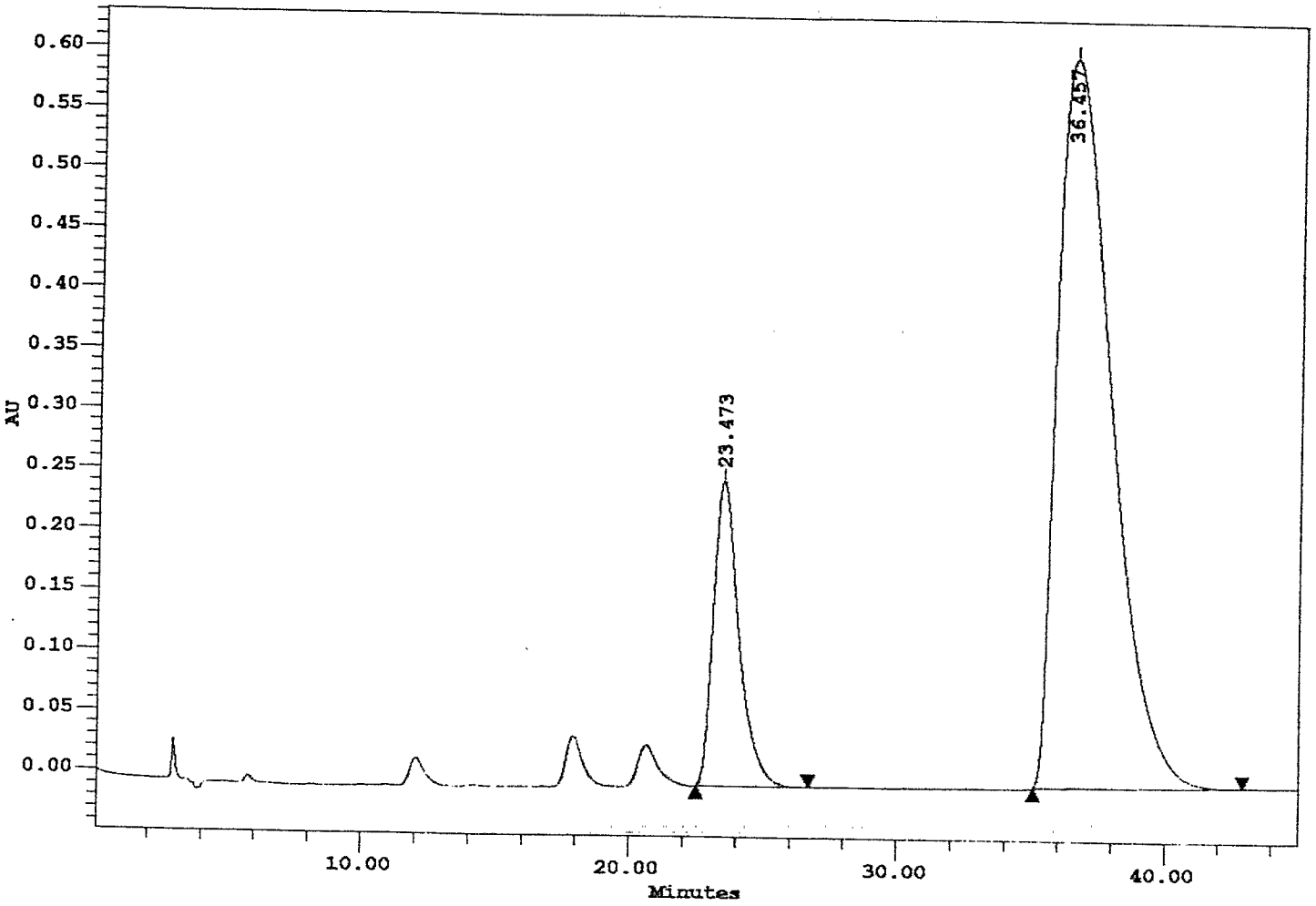
Username SYSTEM | Vial 1 | Acq Meth Set RPH

Colname OJ | solvent hex ipa 9:1 | flowrate 1 ml/min

Structure



(*S*)-**12**



Peak Results

#	Name	Ret Time (min)	Area (uV*sec)	% Area	Height (uV)	Int Type
1	Peak1	23.473	16580150	16.19	252225	BM
2	Peak2	36.457	85860308	83.81	605068	BM

Date Processed 25/09/95 13:12:10

Username SYSTEM

Vial 1

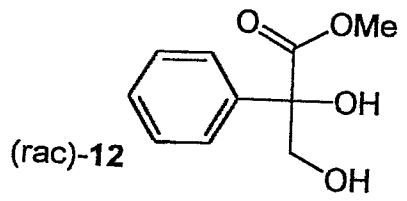
Acq Meth Set Fred_ms

Column Name

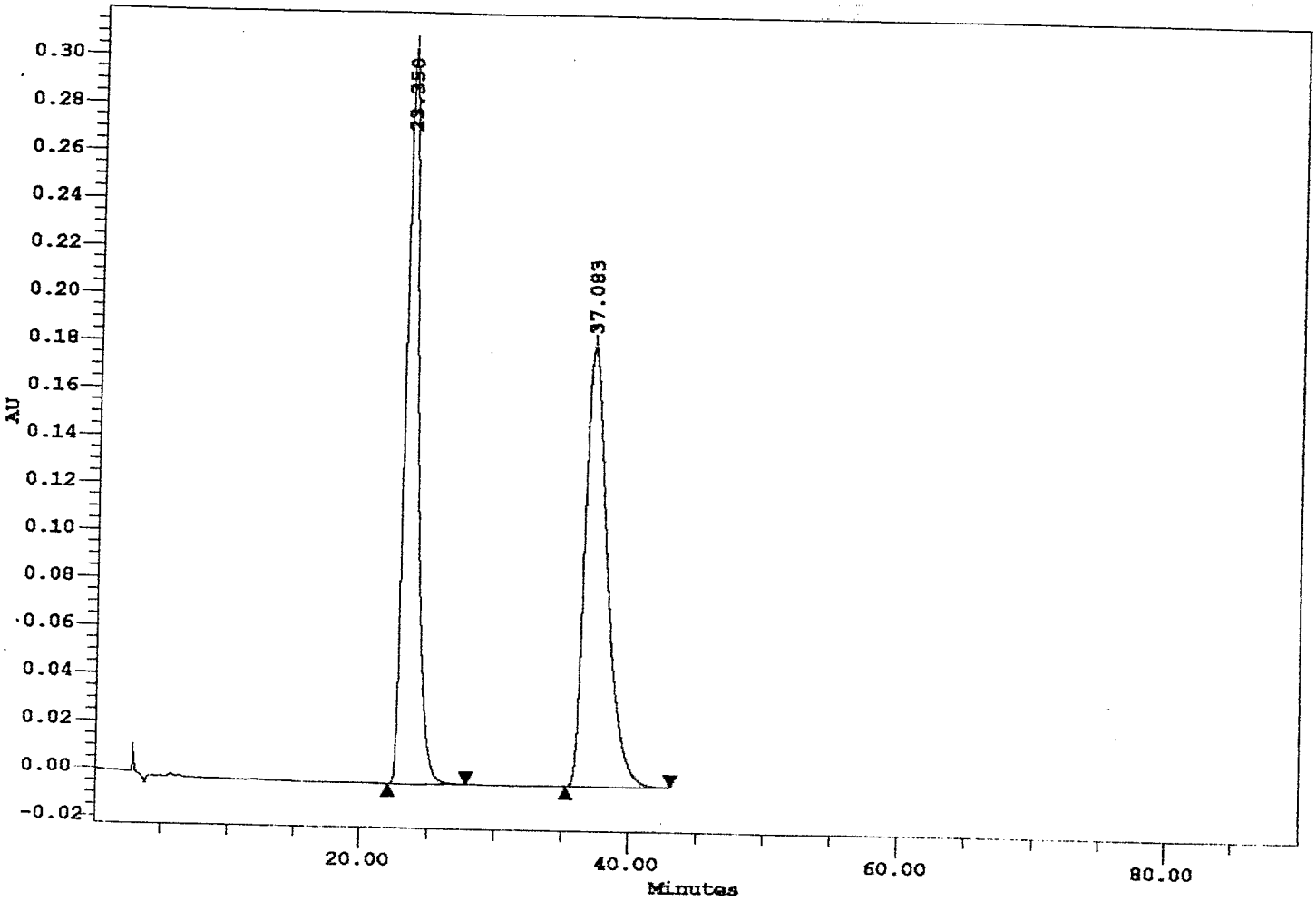
Mobile Phase

Flow Rate

Structure



(rac)-**12**



Peak Results

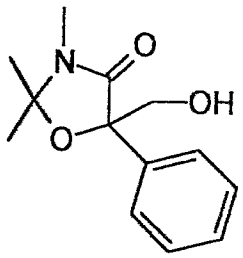
#	Name	Ret Time (min)	Area (uV*sec)	% Area	Height (uV)	Int Type
1	Peak1	23.350	21081378	49.83	308669	BM
2	Peak2	37.083	21223767	50.17	. 184830	BM

Millennium Acquisition Report: ORGChrom RPH Page 1

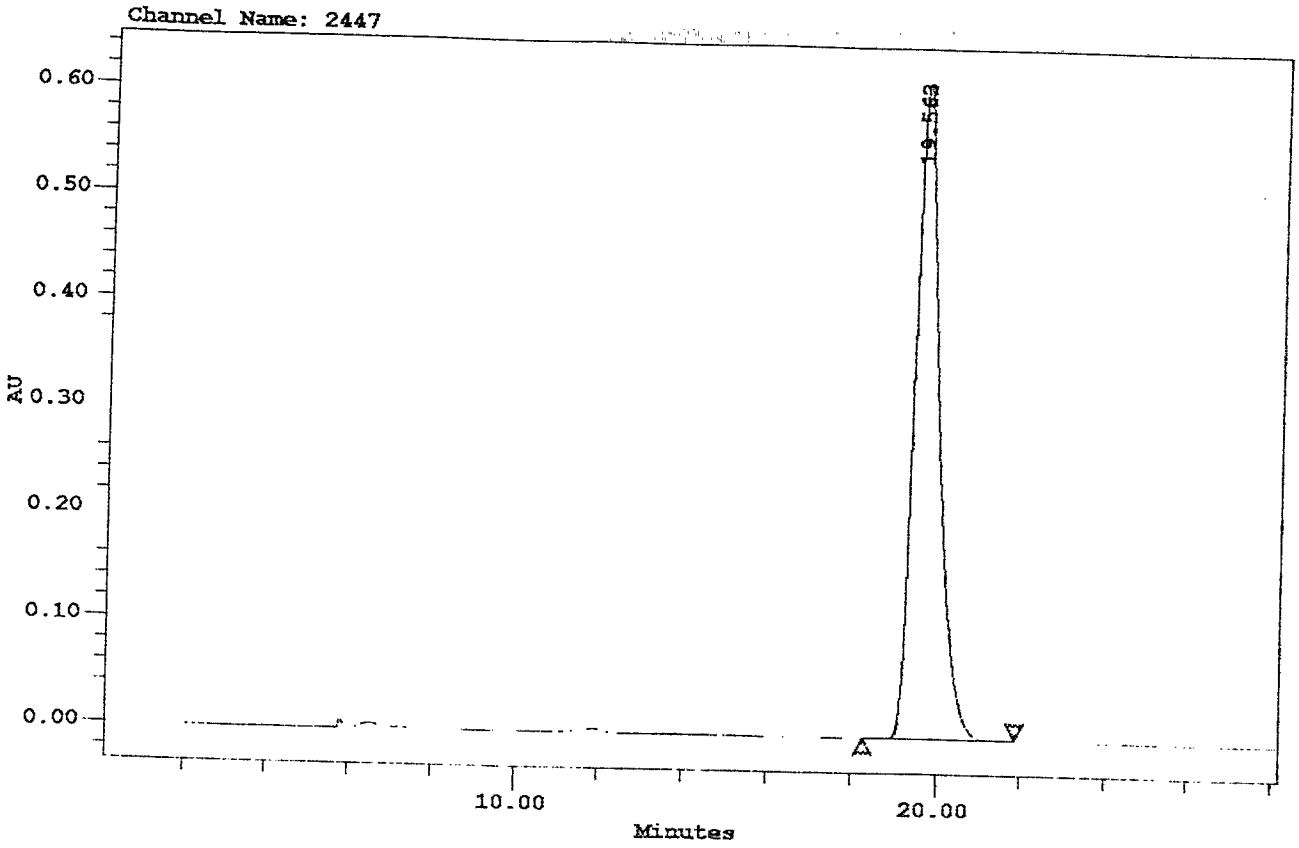
For Sample: NOH Vial: 2 Chan: 991M Date Processed 17/01/95 15:25

MobilePhase: 10% ipa in hex f=.5 ColName: OJ

Struc. Form.



(S)- 10 prepared by CAL resolution



report

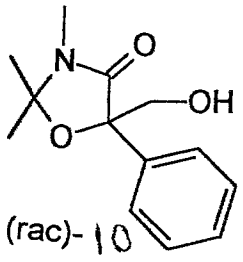
#	Name	Rete Time (min)	TR_PH	Height (uV)	Area (uV*sec)
1	Peak1	19.56	12111197	619076	25249428

Millennium Acquisition Report: ORGChrom Robert Page 1

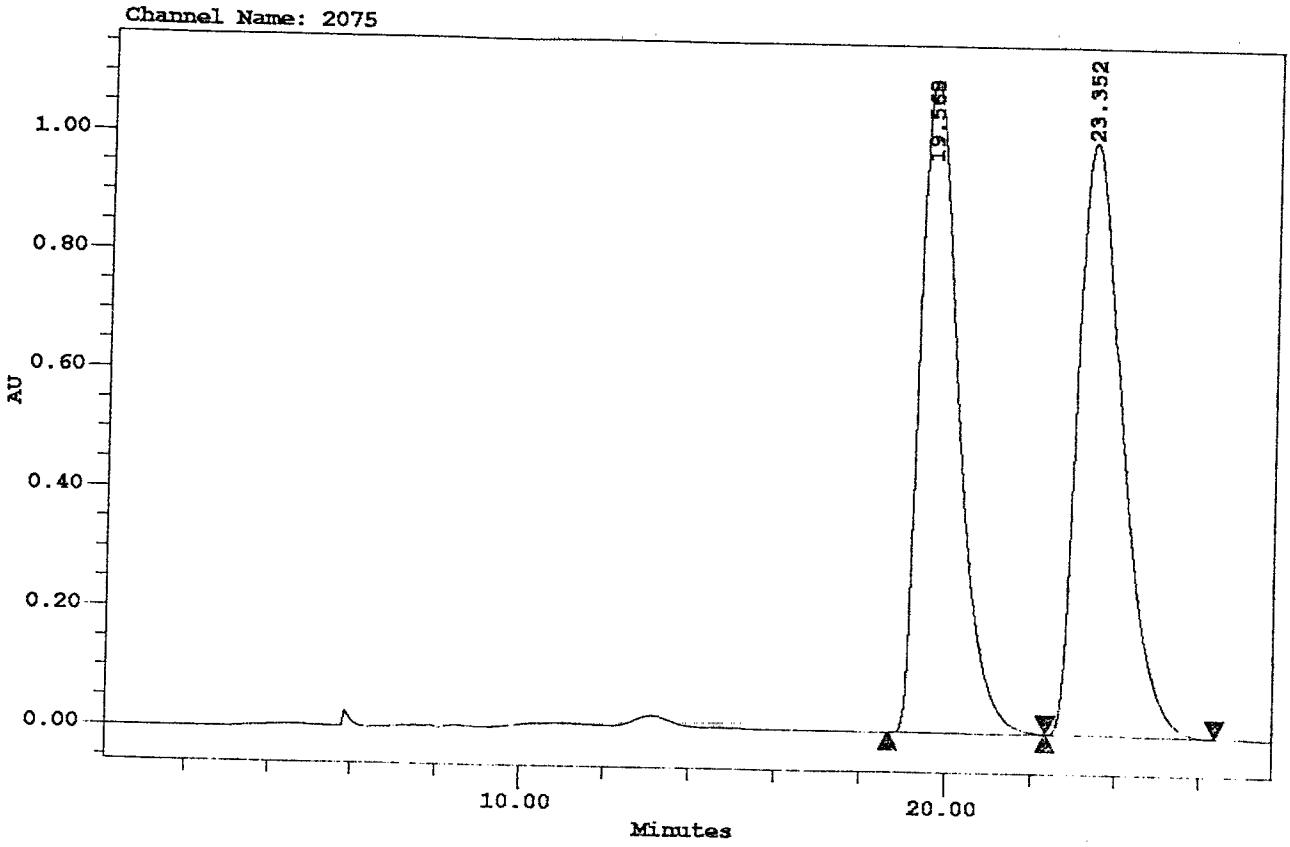
For Sample: dioxolanon Vial: 4 Chan: 991M Date Processed 27/10/94 15:28

MobilePhase: 10% ipa in hex f=.5 ColName: OJ

Struc. Form.



(rac)-10



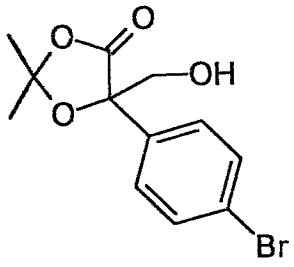
report

#	Name	Rete Time (min)	TR_PH	Height (uV)	Area (uV*sec)
1	Peak1	19.57	21531031	1100300	69748908
2	Peak2	23.35	23341520	999565	73233862

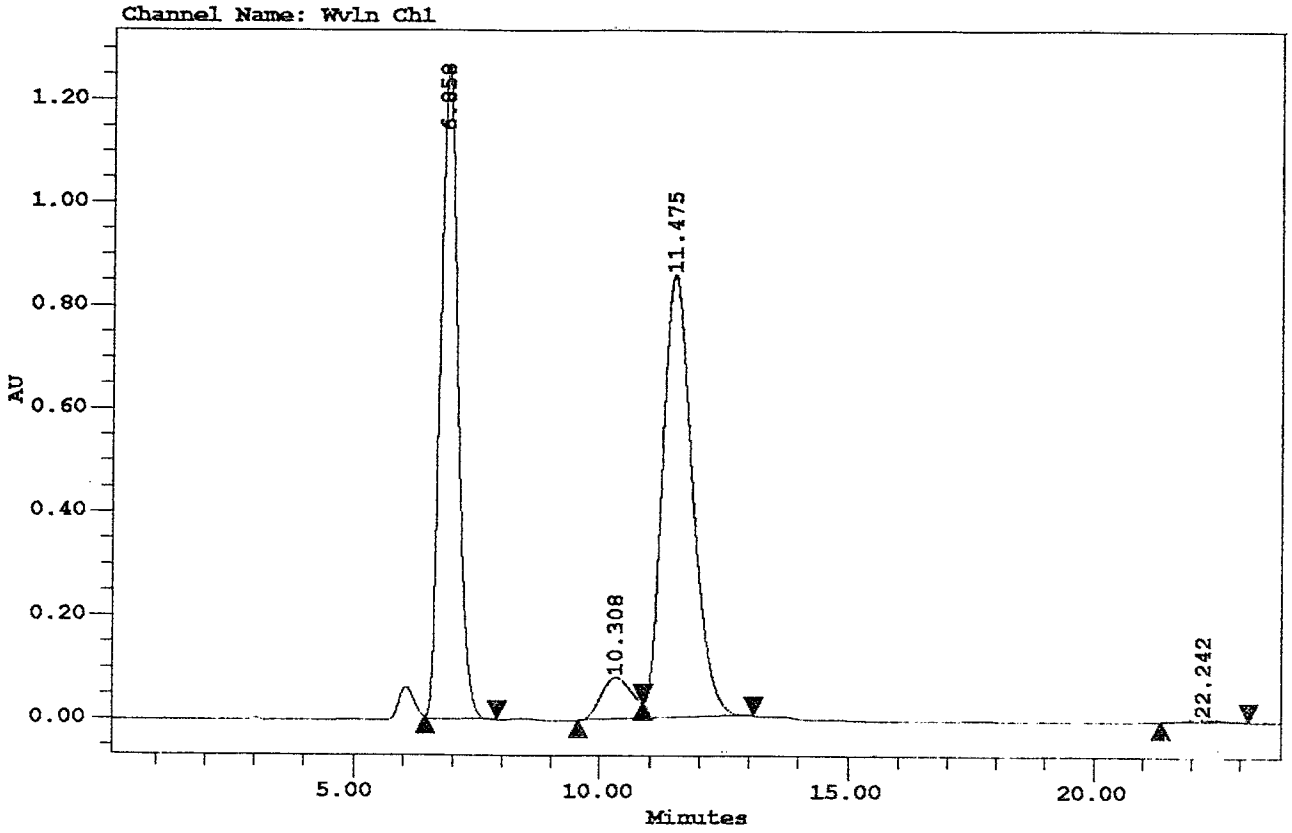
For Sample: brmethyl 5 dag Vial: 1 Chan: 991M Date Processed 11/04/94 15:54

MobilePhase: 20% ipa in hexane ColName: oj

Struc. Form.



(rac)- **b** —CAL, vinyl acetate, dipe→ (*S*)-**2b** (e.e. >98%) + (*R*)-**11b** (e.e. 82%)



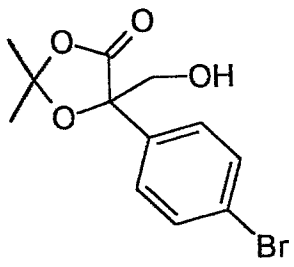
report

*	Name	Rete Time (min)	TR_PH	Height (uV)	Area (uV*sec)
1		6.86	0	1270234	30846958
2		10.31	0	81251	3520144
3		11.48	0	857834	35910466
4		22.24	0	6336	348488

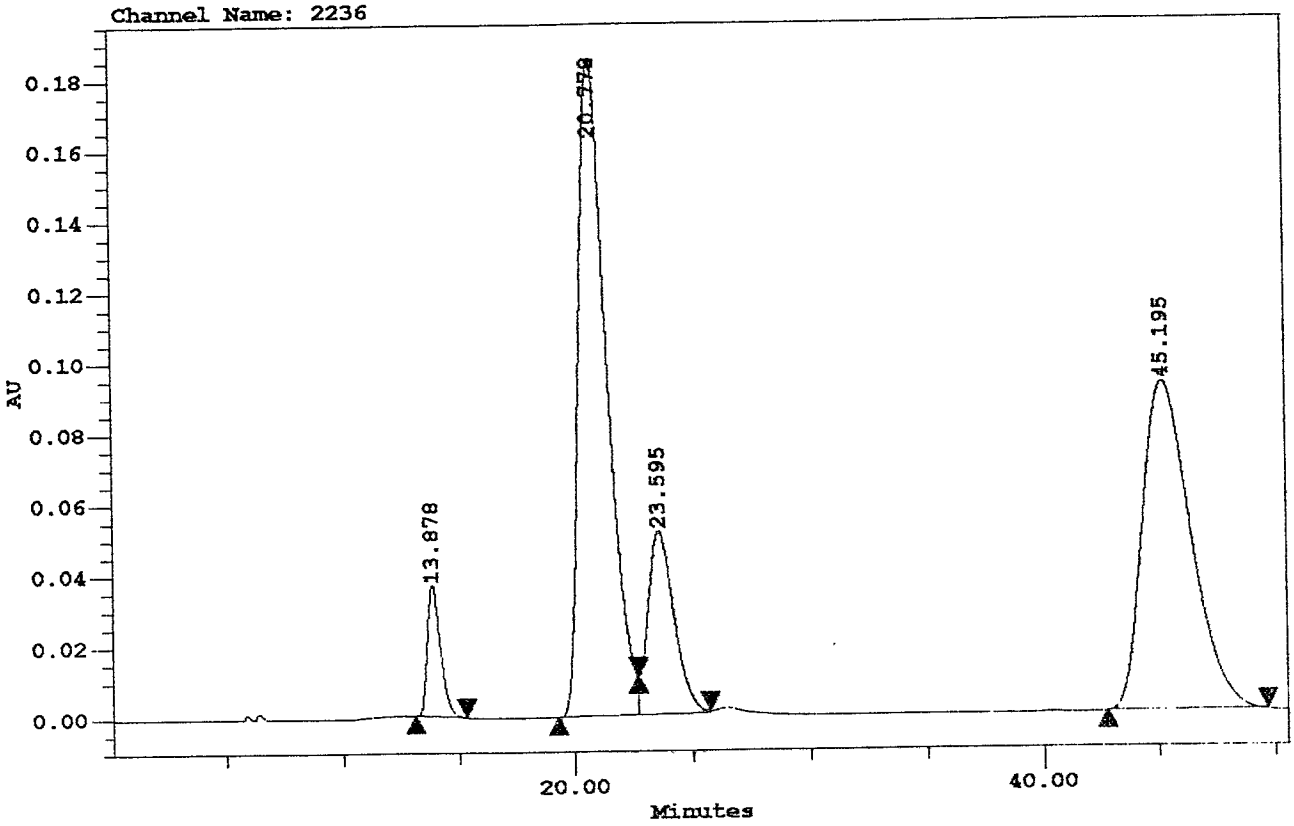
For Sample: p-brCH2OH CC Vial: 1 Chan: 991M Date Processed 07/04/94 13:12

MobilePhase: 20% ipa in hexane ColName: OJ

Struc. Form.

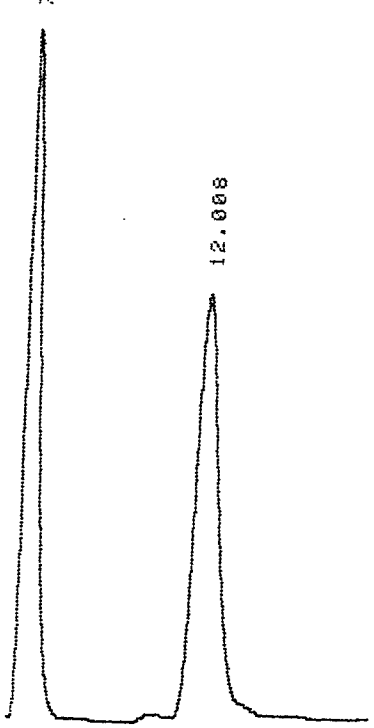


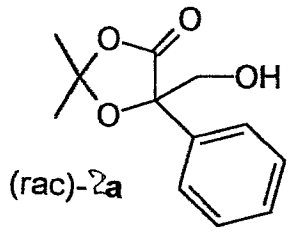
(rac)-**2b** $\xrightarrow[\text{vinyl acetate}]{\text{CCL}}$ (*R*)-**2b** (e.e. 80%) + (*S*)-**11b** (e.e. 60%)



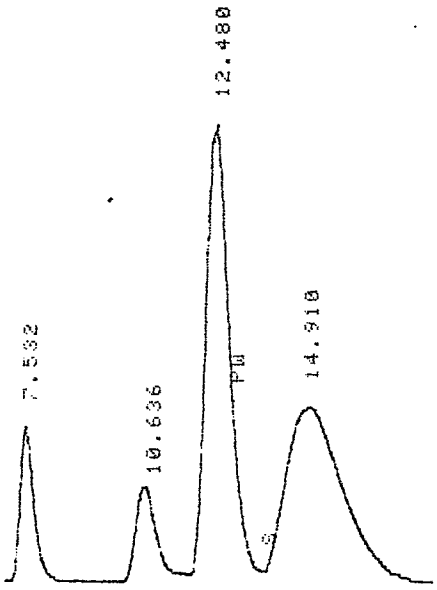
report

#	Name	Rete Time (min)	TR_PH	Height (uV)	Area (uV*sec)
1	Peak1	13.88	512647	36939	1459470
2	Peak2	20.78	3861037	185820	15491997
3	Peak3	23.59	1221203	51757	3934900
4	Peak4	45.19	4182736	92549	13360509



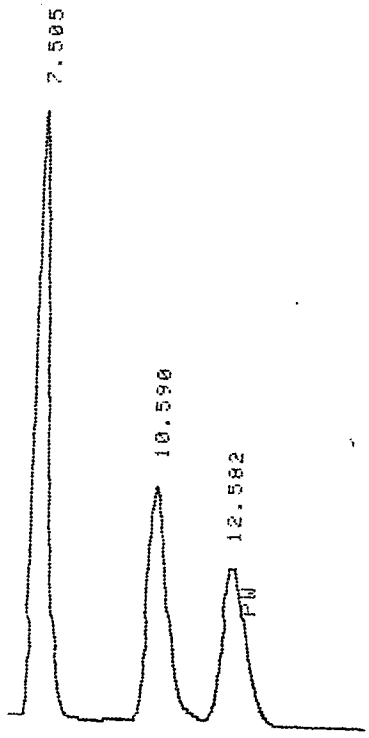


(rac)-2**a**



(rac)-2**a** $\xrightarrow[\text{vinyl acetate}]{\text{CCL}}$ (*R*)-2**a** (e.e. 66%) + (*S*)-**11a** (e.e. 66%)

dipe



(rac)-2**a** $\xrightarrow[\text{vinyl acetate}]{\text{CAL}}$ (*S*)-2**a** (e.e. 37%) + (*R*)-**11a** (e.e. >98%)

dipe